



SEQUENCE LISTING

<10> KUMAGAI, Izumi et al.

<120> NOVEL DIABODY-TYPE BISPECIFIC ANTIBODY

<130> 4600-0106P

<140> US 10/642,284

<141> 2003-08-18

<150> JP 2003-038643

<151> 2003-02-17

<160> 40

<170> PatentIn version 3.1

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<210> 15
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<400> 15
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tca gtg aag ctg ccc tgc aag gct tct ggc gac aca ttc acc agt tac 96
Ser Val Lys Leu Pro Cys Lys Ala Ser Gly Asp Thr Phe Thr Ser Tyr
20 25 30

tgg atg cac tgg gtg aag cag agg cat gga cat ggc cct gag tgg atc 144
Trp Met His Trp Val Lys Gln Arg His Gly His Gly Pro Glu Trp Ile
35 40 45

gga aat att tat cca ggt agt ggt ggt act aac tac gct gag aag ttc 192
Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

aag aac aag gtc act ctg act gta gac agg tcc tcc cgc aca gtc tac 240
Lys Asn Lys Val Thr Leu Thr Val Asp Arg Ser Ser Arg Thr Val Tyr
65 70 75 80

atg cac ctc agc agg ctg aca tct gag gac tct gcg gtc tat tat tgt 288
Met His Leu Ser Arg Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

aca aga tcg ggg ggt ccc tac ttc ttt gac tac tgg ggc caa ggc acc	336
Thr Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr	
100 105 110	

act ctc aca gtc tcc tcc	354
Thr Leu Thr Val Ser Ser	
115	

<210> 26
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1 5 10 15	

gat caa gcc tcc atc tct tgc aga tct agt cag aac att gta cat aat	96
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val His Asn	
20 25 30	

aat gga atc acc tat tta gaa tgg tac ctg caa agg cca ggc cag tct	144
Asn Gly Ile Thr Tyr Leu Glu Trp Tyr Leu Gln Arg Pro Gly Gln Ser	
35 40 45	

cca aag ctc ctg atc tac aaa gtt tcc gac cga ttt tct ggg gtc cca	192
Pro Lys Leu Leu Ile Tyr Lys Val Ser Asp Arg Phe Ser Gly Val Pro	
50 55 60	

gac agg ttc agt ggc agt gga tca ggg aca gat ttc aca ctc aag atc	240
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile	
65 70 75 80	

agc aga gta gag gct gag gat ctg gga att tat tac tgc ttt caa ggt	288
Ser Arg Val Glu Ala Glu Asp Leu Gly Ile Tyr Tyr Cys Phe Gln Gly	
85 90 95	

tca cat att cct ccc acg ttc gga ggg ggg acc aag ctg gaa atc aaa	336
Ser His Ile Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105 110	

cgt gcg	342
Arg Ala	

<210> 27
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 <212> DNA
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<220>
<221> CDS
<222> (1)..(357)
<223> Chimeric Sequence (hOH)

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Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1          5          10          15

agc ctg cgc ctg tct tgc aaa gcg agc ggc tat acc ttt acg cgc tat      96
Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
          20          25          30

acc atg cat tgg gtg cgc cag gcg ccg ggc aaa ggt ctg gaa tgg att      144
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
          35          40          45

ggc tat att aac ccg tct cgc ggc tat acc aac tat aat cag aaa gtg      192
Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
          50          55          60

aaa gat cgc ttt acc att agc cgc gat aac tct aaa aac acc gcg ttt      240
Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
          65          70          75          80

ctg cag atg gat agc ctg cgc ccg gaa gat acc ggc gtg tat ttt tgc      288
Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
          85          90          95

gcg cgc tac tat gat gac cat tat agc ctg gat tat tgg ggc cag ggc      336
Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
          100          105          110

acc ccg gtg acc gtt agc tcg      357
Thr Pro Val Thr Val Ser Ser
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<210> 28
<211> 324
<212> DNA
<213> Artificial Sequence

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<220>
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<222> (1)..(324)
<223> Chimeric Sequence (hOL)

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1          5          10          15

gat cgc gtg acc att acg tgc agc gcg tct agc tct gtg agc tat atg      96
Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met

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	20	25	30	
aac tgg tac cag caa acc cca ggc aaa gcg ccg aaa cgc tgg att tat				144
Asn Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr				
	35	40	45	
gat acc agc aaa ctg gcg agc ggc gtg ccg agc cgc ttt agc ggc tct				192
Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser				
	50	55	60	
ggt agc ggc acc gat tat acg ttt acc att agc tct ctg cag ccg gaa				240
Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu				
	65	70	75	80
gat att gcg acc tat tac tgc cag caa tgg agc tct aac ccg ttt acc				288
Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr				
	85	90	95	
ttt ggc cag ggt acc aaa ctg cag att acc cgc gcg				324
Phe Gly Gln Gly Thr Lys Leu Gln Ile Thr Arg Ala				
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala				
1	5	10	15	
tcg gtt aaa gtg agc tgc aaa gcc tca ggc tat acc ttt acg agc tac				96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr				
	20	25	30	
tgg atg cat tgg gtg cgc cag gcc ccg ggt cag ggc ctg gaa tgg atg				144
Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met				
	35	40	45	
ggt aac att tat ccg ggc agc ggt ggc acc aac tat gcg gaa aaa ttt				192
Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe				
	50	55	60	
aag aac cgc gtg acc atg acg cgt gat acc agc att tcg acg gcc tat				240
Lys Asn Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr				
	65	70	75	80
atg gaa ctg agc cgc ctg cgt agc gat gac acc gcc gtg tat tac tgc				288
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys				
	85	90	95	

gcg cgc agt ggc ggt ccg tat ttt ttc gat tac tgg ggc cag ggt acg	336
Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr	
100 105 110	

ctg gtt acc gtg agc tcg	354
Leu Val Thr Val Ser Ser	
115	

<210> 30
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 <222> (1)..(342)
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1 5 10 15	

gaa ccg gcg tcg att agc tgc cgc agc tcg cag aac atc gtg cat aat	96
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val His Asn	
20 25 30	

aac ggc att acc tat ctg gaa tgg tat ctg cag aaa ccg ggc caa agc	144
Asn Gly Ile Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser	
35 40 45	

ccg cag ctg tta att tat aaa gtg agc gat cgc ttt agc ggc gtg ccg	192
Pro Gln Leu Leu Ile Tyr Lys Val Ser Asp Arg Phe Ser Gly Val Pro	
50 55 60	

gat cgc ttt tcg ggc agc ggt agt ggc acc gat ttt acg ctg aaa att	240
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile	
65 70 75 80	

agc cgc gtg gaa gcg gag gat gtt ggc gtg tat tac tgc ttt cag ggc	288
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly	
85 90 95	

agc cat atc ccg cca acc ttt ggc caa ggc acc aaa gtg gaa att aaa	336
Ser His Ile Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys	
100 105 110	

cgc gcg	342
Arg Ala	

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<223> Chimeric Sequence (h5H-m01)

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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<212> PRT

<213> Artificial Sequence

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<223> Chimeric Sequence (h5H-m02)

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Thr
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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<212> PRT
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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<212> PRT
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<223> Chimeric Sequence (h5H-m04)

<400> 34

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Asp Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Thr
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Lys Val Thr Leu Thr Val Asp Arg Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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<220>
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1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Lys Val Thr Leu Thr Val Asp Arg Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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<212> PRT
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<220>
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<400> 39

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Lys Val Thr Leu Thr Val Asp Arg Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Thr
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
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1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Ala Glu Lys Phe
50 55 60

Lys Asn Lys Val Thr Met Thr Val Asp Thr Ser Ser Arg Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Thr
85 90 95

Ala Arg Ser Gly Gly Pro Tyr Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115